Stress ossidativo nella Malattia di Fabry: implicazioni per il rimodellamento cardiovascolare

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Fabry disease is characterized by deficient expression/activity of α-GalA with consequent lysosomal accumulation in various organs of its substrate Gb3. Despite enzyme replacement therapy, Fabry disease progresses with serious myocardial, cerebral and renal manifestations. Gb3 accumulation may induce oxidative stress (OxSt), production of inflammatory cytokines and reduction of nitric oxide, which may impact on Fabry disease’s clinical manifestations.

OxSt status was characterized in 10 patients compared with 10 healthy subjects via protein expression of p22phox, subunit of NADH/NADPH oxidase, (Western blot), Heme oxygenase (HO)-1 levels (ELISA), antioxidant/anti-inflammatory, lipid peroxidation as malondialdehyde (MDA) production (colorimetric assay), phosphorylation state of Extracellular Signal Regulated Kinase (ERK)1/2 and Myosin Phosphatase Target Protein (MYPT)-1 (Western blot), marker of Rho kinase activation, both involved in OxSt signaling. Cardiac left ventricular (LV) mass was also evaluated (M-mode echocardiography).

LV mass was higher in Fabry’s males (123.72±2.87g/m²) and females (132.09±11.65g/m²). p22phox expression was also higher in patients (1.04±0.12 d.u vs 0.48±0.05, p=0.01) as well as MDA levels (54.51±4.43 vs 30.05±7.94nmol/mL, p=0.01) while HO-1 was reduced (8.57±1.03 vs 14.03±1.60ng/mL p=0.02). MYPT-1’s phosphorylation was increased in patients (1.79±0.23d.u vs 1.06±0.13, p<0.05) while phosphorylation of ERK1/2 was reduced (0.91±0.08 vs 1.53±0.17, p=0.004).

This study documents OxSt activation and the altered reaction to it in Fabry patients. Cardiac remodeling, Rho kinase signaling activation and reduction of protective HO-1 might suggest that, in addition to enzyme replacement therapy, OxSt inhibition by either pharmacological or nutritional measures, is likely to prove useful for the prevention/treatment of Fabry patients’ cardiovascular-renal remodeling.